

Notice of Allowability

Application No.

10/688,193

Examiner

Suzanne M. Noakes, Ph.D.

Applicant(s)

WOODS, VIRGIL L.

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the response filed the 16th of April 2007 and the proposed Ex. Amendments of record.
2. ☒ The allowed claim(s) is/are 1-42.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>20070501</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____ |

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Stephen Reiter on 14 May 2007.

The application has been amended as follows:

In the claims:

Rewrite claim 1: A method for improving the success of crystallizing a protein or improving the quality of a crystallized protein for crystallographic structure determination thereof, said method comprising:

- (a) identifying at least one unstructured region of said protein by hydrogen exchange analysis;
- (b) deleting at least one unstructured region of said protein identified by hydrogen exchange analysis; and
- c) subjecting to crystallization and structure determination one or more modified form(s) of said protein according to step (b).

- Cancel claims 43-48.

Restriction/Election

2. The requirement for an election of species between endopeptidases and carboxypeptidases is hereby withdrawn. Specifically claims 18 and 19 have been rejoined. Furthermore, the restriction requirement between claims 1-43 and claim 44 is hereby withdrawn. However, it appears that claim 44 is substantial duplicate of claims 1 and 41 and thus, as noted above, has been cancelled. The restriction requirement between claims 1-43 (Group I) and claims 45 (Group III), 46-47 (Group IV) and 48 (Group V) as detailed in the Office action dated 04 April 2006 is maintained. Said claims have been cancelled by Examiner's amendment as noted above.

Reason's for Allowance

3. The following is an examiner's statement of reasons for allowance: The science of protein crystallography is at best unpredictable and more of an art than a science. Many different factors contribute to the unpredictability and these are outlined, for example, in MacPherson, A. (Current Approaches to Macromolecular Crystallization, European Journal of Biochemistry, 1990, Vol. 189, pp. 1-23), who states there are 25 different parameters that influence the crystallization of any given protein, however, knowing which ones are the essential factors for any particular protein is never clear and can not be inferred. There are some techniques which are known that may increase the chance that protein will crystallize such as manipulating the N-terminus or C-terminus which are often times are not well ordered and at times can preclude crystallization of a protein. However, what makes the instant methods novel over the

prior art is the ability to determine exactly, down to single amino acids, which regions are unstructured. This gives an enormous advantage to the protein crystallographer to improve the chances that a protein might crystallize because it is well known that unstructured regions are not limited to only the C- or N-terminus' and often times can be found anywhere in a protein. These unstructured regions are often times considered to be one of the largest obstacles to successful crystallization. However, to date, other than protein crystallography itself, or NMR methods, which are methods to determine the 3-D structures which would then give clues to where the unstructured regions exist, there are no other methods to detail these unstructured regions. Herein lies the problem, however, when the protein a skilled artisan is working with does not crystallize and there is no analogous structure, how does one know where the unstructured regions exist, or if they exist at all? Although the method of hydrogen exchange analysis has been known for many years, the method has mainly been utilized in determining the steps involved in protein folding. The leap from protein folding to protein crystallization and improving the chances that a protein will crystallize or improving the quality of a protein that has already been crystallized by deleted the unstructured regions is both novel and non-obvious. **The allowed claims are 1-42.**

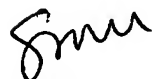
Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

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4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Noakes, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached on Monday to Friday, 7.00am to 3.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



SMN
14 May 2007



KATHLEEN KERR BRAGDON, PH.D.
SUPERVISORY PATENT EXAMINER